AMENDMENTS

A Version With Markings to Show Changes Made follows Applicant's Remarks beginning at page 15.

In the Claims:

Please amend Claims 1 and 15, and add new claims 49-66, as follows.

1. (Thrice Amended) An in vitro method of transdifferentiating an epidermal basal cell into a cell having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell, comprising:

(a) culturing a proliferating epidermal basal cell population comprising one or more epidermal basal cell(s), said cell(s) derived from the skin of a mammalian subject;

(b) exposing the cell(s) to an amount of an antagonist of bone morphogenetic protein (BMP) effective to antagonize endogenous BMP signal transduction activity;

(c) growing the cell(s) in the presence of at least one antisense oligonucleotide comprising a segment of a human MSX1 gene and/or a segment of a human HES1 gene, or homologous non-human counterpart of either of these, in an amount effective to suppress the expression of functional gene product of MSX1 and/or HES1, whereby the cell is transdifferentiated into a cell having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell; and

(d) growing the transdifferentiated cell in a medium comprising a retinoid compound and a signal molecule selected from the group consisting of brain-derived neurotrophic factor (BDNF), ciliary neurotrophic factor (CNTF), platelet-derived growth factor (PDGF), nerve growth factor (NGF), neurotrophin (NT)-3, neurotrophin (NT)-4, IL-6, sonic hedgehog, and sonic hedgehog aminoterminal peptide, wherein:

(i) said signal molecule, being selected from the group consisting of sonic hedgehog and sonic hedgehog aminoterminal peptide, the physiological and/or immunological

feature comprises expression of a neural progenitor cell marker selected from the group consisting of nestin and neural RNA-binding protein Musashi, or a combination of these;

(ii) said signal molecule, being selected from the group consisting of brain-derived neurotrophic factor (BDNF), platelet derived growth factor (PDGF), nerve growth factor (NGF), sonic hedgehog, sonic hedgehog aminoterminal peptide, neurotrophin (NT)-3, and neurotrophin (NT)-4, the physiological and/or immunological feature comprises expression of a neuronal cell marker selected from the group consisting of neurofilament M, neural-specific β-tubulin, neural-specific enolase, and microtubule associated protein 2, or a combination of any of these; and wherein the morphological feature comprises one or more morphological neurite-like process(es) at least about 50 micrometers in length; and

(iii) said signal molecule, being selected from the group consisting of ciliary neurotrophic factor (CNTF), IL-6, sonic hedgehog, and sonic hedgehog aminoterminal peptide, the physiological and/or immunological feature comprises expression of a glial cell marker selected from the group consisting of glial fibrillary acidic protein (GFAP) and O4.

2. (Reiterated) The method of Claim 1, wherein the subject is a human.

3. (Reiterated) The method of Claim 1, wherein the epidermal basal cell(s) is derived from a skin biopsy.

4. (Reiterated) The method of Claim 1, wherein culturing the proliferating epidermal basal cell population further comprises separating keratinized epidermal cells from the epidermal basal cells in a calcium-free medium.

5. (Reiterated) The method of Claim 1, wherein the amount of the antagonist of bone morphogenetic protein is about 10^{-6} to 10^{-4} M.

6. (Reiterated) The method of Claim 5, wherein the amount of the antagonist of bone morphogenetic protein is about 5 x 10^{-6} to 5 x 10^{-5} M.

7. (Reiterated) The method of Claim 1, wherein the antagonist of bone morphogenetic protein (BMP) is fetuin, noggin, chordin, gremlin, or follistatin.

8. (Reiterated) The method of Claim 7, wherein the fetuin is mammalian or avian fetuin.

N.E.

9. (Reiterated) The method of Claim 8, wherein the mammalian fetuin is human, bovine, porcine, ovine, or equine fetuin.

10. (Reiterated) The method of Claim 1, wherein the antisense oligonucleotide(s) is modified with one or more thio groups.

11. (Reiterated) The method of Claim 1, wherein the amount of the antisense oligonucleotide is about 5 x 10^{-6} M to about 10^{-5} M.

13. (Reiterated) The method of Claim 1, wherein the morphological feature comprises one or more morphological neurite-like process(es) at least about 50 micrometers in length.

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15. (Amended) The method of Claim 1, wherein the retinoid compound is all-trans retinoic acid or Vitamin A.

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17. (Reiterated) A transdifferentiated cell of epidermal origin having one or more

morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell produced by the method of Claim 1.

19. (Reiterated) The transdifferentiated cell of Claim 17, wherein the cell further exhibits a lack of mitotic activity under cell culture conditions which induce differentiation in neural progenitor cells.

20. (Reiterated) The cell of Claim 17, wherein the transdifferentiated cell has a morphological, physiological and/or immunological feature specific to a neuronal cell.

22. (Reiterated) The transdifferentiated cell of Claim 20, wherein the cell is a GABAergic cell.

23. (Reiterated) The transdifferentiated cell of Claim 20, wherein the cell is a dopaminergic cell.

24. (Reiterated) The transdifferentiated cell of Claim 17, wherein the morphological feature comprises one or more neurite-like process(es) at least about 50 micrometers in length.

25. (Reiterated) The cell of Claim 17, wherein the transdifferentiated cell has a morphological, physiological, or immunological feature specific to an astroglial or oligodendroglial cell.

26. (Reiterated) The transdifferentiated cell of Claim 25, wherein the immunological feature comprises expression of glial fibrillary acidic protein (GFAP) or O4.

27. (Reiterated) The transdifferentiated cell of Claim 17, wherein the cell is of human origin.

28. (Reiterated) A cell culture derived from the transdifferentiated cell of Claim 17, comprising a plurality of cells that express one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell.

29. (Reiterated) A transdifferentiated cell of epidermal origin and cultured in vitro, comprising a cell of epidermal basal cell origin, said transdifferentiated cell displaying one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell, wherein the physiological and/or immunological feature comprises expression of a marker selected from the group consisting of nestin, neural RNA-binding protein Musashi, neurofilament M, neural-specific β-tubulin, neural-specific enolase, microtubule associated protein 2, glial fibrillary acidic protein (GFAP), O4, or a combination of any of these.

30. (Reiterated) The transdifferentiated cell of Claim 29, wherein the cell further displays the physiological feature of a lack of mitotic activity under cell culture conditions which induce differentiation in neural progenitor cells.

31. (Reiterated) The cell of Claim 29, wherein the transdifferentiated cell has a morphological, physiological, or immunological feature specific to a neuronal cell.

32. (Reiterated) The transdifferentiated cell of Claim 31, wherein the physiological and/or immunological feature comprises expression of neural RNA-binding protein Musashi, neurofilament M, neural-specific β-tubulin, neural-specific enolase, microtubule associated protein 2.

33. (Reiterated) The transdifferentiated cell of Claim 31, wherein the cell is a GABAergic cell.

34. (Reiterated) The transdifferentiated cell of Claim 31, wherein the cell is a dopaminergic cell.

35. (Reiterated) The transdifferentiated cell of Claim 29, wherein the morphological feature comprises one or more neurite-like process(es) at least about 50 micrometers in length.

36. (Reiterated) The transdifferentiated cell of Claim 29, wherein the cell is of human origin.

37. (Reiterated) The cell of Claim 29, wherein the transdifferentiated cell has a morphological, physiological, or immunological feature specific to an astroglial or oligodendroglial cell.

38. (Reiterated) The transdifferentiated cell of Claim 37, wherein the physiological and/or immunological feature comprises expression of glial fibrillary acidic protein (GFAP) or O4.

39. (Reiterated) A cell culture derived from the transdifferentiated cell of Claim 29, comprising a plurality of cells that express one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell.

43. (Reiterated) A kit for transdifferentiating, in vitro, an epidermal basal cell into a cell having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell, comprising:

(A) an antagonist of bone morphogenetic protein (BMP);

(B) at least one antisense oligonucleotide comprising a segment of a human MSX1 gene, a segment of a human HES1 gene, or a non-human homologous counterpart of either of these; and

(C) a retinoid compound and a signal molecule selected from the group consisting of brain-derived neurotrophic factor (BDNF), ciliary neurotrophic factor (CNTF), platelet-derived growth factor (PDGF), nerve growth factor (NGF), neurotrophin (NT)-3, neurotrophin (NT)-4, IL-6, sonic hedgehog, and sonic hedgehog aminoterminal peptide.

44. (Reiterated) The kit of Claim 43, further comprising instructions for using (A), (B), and (C) in transdifferentiating a subject's epidermal basal cell(s).

45. (Reiterated) The kit of Claim 43, wherein the antagonist of bone morphogenetic protein (BMP) is fetuin, noggin, chordin, gremlin, or follistatin.

47. (Reiterated) The kit of Claim 43, wherein the retinoid compound is all-trans retinoic acid or Vitamin A.

Please Add New Claims 49-65 as follows:

--49. (New) An in vitro method of transdifferentiating an epidermal basal cell into a cell having one or more morphological, physiological and/or immunological feature(s) of a neuronal cell, comprising:

(a) culturing a proliferating epidermal basal cell population comprising one or more epidermal basal cell(s), said cell(s) derived from the skin of a mammalian subject;

(b) exposing the cell(s) to an amount of an antagonist of bone morphogenetic protein (BMP) effective to antagonize endogenous BMP signal transduction activity;

(c) growing the cell(s) in the presence of at least one antisense oligonucleotide comprising a segment of a human MSX1 gene and/or a segment of a human HES1 gene, or homologous non-human counterpart of either of these, in an amount effective to suppress the expression of functional gene product of MSX1 and/or HES1, whereby the cell is transdifferentiated into a cell having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell; and

(d) growing the transdifferentiated cell in a medium comprising a retinoid compound and a signal molecule selected from the group consisting of brain-derived neurotrophic factor (BDNF), platelet-derived growth factor (PDGF), nerve growth factor (NGF), neurotrophin (NT)-3, neurotrophin (NT)-4;

wherein the physiological and/or immunological feature comprises expression of a neuronal cell marker selected from the group consisting of neurofilament M, neural-specific β-tubulin, neural-specific enolase, and microtubule associated protein 2, or a combination of any of these; and

wherein the morphological feature comprises one or more morphological neurite-like process(es) at least about 50 micrometers in length.

50. (New) The method of Claim 49, wherein the subject is a human.

51. (New) The method of Claim 49, wherein the epidermal basal cell(s) is derived from a skin biopsy.

52. (New) The method of Claim 49, wherein culturing the proliferating epidermal

basal cell population further comprises separating keratinized epidermal cells from the epidermal basal cells in a calcium-free medium.

53. (New) The method of Claim 49, wherein the amount of the antagonist of bone morphogenetic protein is about 10^{-6} to 10^{-4} M.

54. (New) The method of Claim 53, wherein the amount of the antagonist of bone morphogenetic protein is about 5×10^{-6} to 5×10^{-5} M.

55. (New) The method of Claim 49, wherein the antagonist of bone morphogenetic protein (BMP) is fetuin, noggin, chordin, gremlin, or follistatin.

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56. (New) The method of Claim 55, wherein the fetuin is mammalian or avian fetuin.

57. (New) The method of Claim 56, wherein the mammalian fetuin is human, bovine, porcine, ovine, or equine fetuin.

58. (New) The method of Claim 49, wherein the antisense oligonucleotide(s) is modified with one or more thio groups.

59. (New) The method of Claim 49, wherein the amount of the antisense oligonucleotide is about 5×10^{-6} M to about 10^{-5} M.

60. (New) The method of Claim 49, wherein the retinoid compound is all-trans retinoic acid or Vitamin A.

61. (New) A transdifferentiated cell of epidermal origin having one or more morphological, physiological and/or immunological feature(s) of a neuronal cell produced by the method of Claim 49, wherein the physiological and/or immunological feature comprises expression of a marker selected from the group consisting of neurofilament M, neural-specific β-tubulin, neural-specific enolase, and microtubule associated protein 2, or a combination of any of these; and wherein the morphological feature comprises one or more morphological neurite-like process(es) at least about 50 micrometers in length.

62. (New) The transdifferentiated cell of Claim 61, wherein the cell further exhibits a lack of mitotic activity under cell culture conditions which induce differentiation in neural progenitor cells.

F 3 cont'd

63. (New) The transdifferentiated cell of Claim 61, wherein the cell is a GABAergic cell.

64. (New) The transdifferentiated cell of Claim 61, wherein the cell is a dopaminergic cell.

65. (New) The transdifferentiated cell of Claim 61, wherein the cell is of human origin.

66. (New) A cell culture derived from the transdifferentiated cell of Claim 61, comprising a plurality of cells that express one or more morphological, physiological and/or immunological feature(s) of a neuronal cell.--.